# A prospective study in the Australian petroleum industry. II Incidence of cancer

D Christie, K Robinson, I Gordon, J Bisby

# Abstract

This paper reports incidence of cancer in employees of the Australian petroleum industry from 1981 to 1989. Two surveys by personal interview incorporated more than 15 000 employees, representing 92% of the eligible population. Subjects were included in the analysis after completing five years of service in the industry. At the time of this report the cohort did not include sufficiently large numbers of women for useful analysis; results presented are restricted to the men. On 31 December 1989, 50 254 person-years of observation had accumulated in the men with 152 incident cancers reported. The standardised incidence ratio (SIR) analysis showed overall cancer rates close to those of the national population. Whereas deficits were seen in some cancer sites, notably lung cancer (SIR 0.5, 95% confidence interval (95% CI) 0.3-0.9), incidence rates for some other cancer sites suggested increased risk. An excess of observed over expected cases was present in all subcategories of lymphohaematopoietic cancer except Hodgkin's disease (no cases), and was most apparent in myeloid leukaemia (SIR 4.0, 95% CI 1.6-8.2). The other major site with a raised number of cases observed over expected was melanoma (SIR 1.4, 95% CI 0.8-2.1).

With the exception of one American study<sup>1</sup> of short duration and the Australian study that is the subject of this paper, the numerous epidemiological studies carried out within the petroleum industry have been of the historical cohort design with mortality as the

Department of Community Medicine, The University of Melbourne, Australia K Robinson, J Bisby

Statistical Consulting Centre, The University of Melbourne, Australia I Gordon endpoint. In an accompanying paper a prospective cohort study in the Australian petroleum industry (Health Watch) is described with mortality results to 31 December 1989.<sup>2</sup> This paper also monitors incidence of cancer in the cohort using data from population based cancer registries that have been established in each state and territory of Australia from 1982 or earlier.

As an endpoint in studies of cancer, incidence has certain advantages over mortality. When another cause of death supervenes, there can be no guarantee that the certifying physician will include cancer on the certificate. Furthermore, incidence is a direct reflection of the occurrence of cancer regardless of survival. Thus incident cancers present greater numbers for study over an equivalent time period. As persons and institutions responsible for diagnosing cancer in Australia are legally required to report each cancer to the applicable state registry with sufficient information relating to morphology, topography, and differentiation to permit detailed classification, the opportunities for classification errors are reduced.

In this paper the incidence of various cancers in a petroleum industry cohort is compared with that expected in the Australian national population and internal comparisons are also made.

# Methods

A description of the composition and the methods of study of the cohort are given in the preceding paper in this journal, which considers mortality.<sup>2</sup> Modifications to study incidence of cancer are described below.

Follow up of the population has been maintained through company records for those still employed and by annual mail contact for those who have left the industry. The names of all members of the study population have been matched annually with the appropriate population based state cancer registry. With the exception of melanomas, skin cancers are not recorded by the registries.

As the state cancer registries have differing time lags in their reporting, person-years at risk are calculated for each state for only the period for which its registry declares the calendar year complete. Thus fewer person-years are available for analysis of cancer incidence than for mortality.

**Discipline of Environment and Occupational Health The University of Newcastle, Australia** D Christie

Table 1 Incidence for major cancer sites: men

Malignant neoplasm of :	ICD-9	Observed	Expected	SIR (95% CI)
Lip	140	6	5.5	1.1  (0.4 - 2.4)
Salivary gland	142	2	0.7	2.9 (0.4 - 11)
Oropharynx	146	2	1.4	1.4 (0.2 -5.1)
Stomach	151	6	6.2	1.0  (0.4 - 2.1)
Colon	153	13	13.0	1.0 (0.5 - 1.7)
Rectum	154	8	9.0	0.9 (0.4 -1.8)
Liver	155	2	1.3	1.5 (0.2 -5.5)
Pancreas	157	4	4.2	1.0 (0.3 -2.5)
Larvnx	161	4	4.4	0.9 (0.2 - 2.3)
Lung	162	15	28.6	0.5 (0.3 -0.9)
Other respiratory	163-5	2	1.1	1.8 (0.2 - 6.6)
Connective tissue	171	3	1.3	2.4 (0.5 -6.9)
Melanoma	172	20	14.4	1.4 (0.8 -2.1)
Prostate	185	8	8.1	1.0 (0.4 - 1.9)
Testis	186	3	3.1	1.0  (0.2 - 2.8)
Bladder	188	10	7.9	1.3 (0.6 -2.3)
Kidney	189	4	4.6	0.9 (0.2 - 2.2)
Brain	191	3	4.4	0.7 (0.1 - 2.0)
Non-Hodgkin's lymphoma	200 and 202	10	5.9	1.7 (0.8 -3.1)
Multiple myeloma	203	4	1.8	2.2 (0.6 -5.6)
Leukaemia	204-208	12	3.6	3.4 (1.7 -5.9)
Lymphoid	204	4	1.4	2.9 (0.8 -7.5)
Myeloid	205	7	1.8	4.0 (1.6 -8.2)
Other leukaemia	206-208	1	0.4	2.3 (0.1 -13)
Other sites		11	22.7	()
All sites		152	153.0	0.99 (0.84-1.16)

Note: Leukaemias appear both grouped and separately.

Standardised incidence ratios (SIRs) have been calculated using the pooled Australian State Cancer Registry statistics for 1982 as reference, these being the only Australian pooled data available at present. Cancer registries of Australian states use the ninth revision of the International Classification of Diseases (ICD9). The usual Poisson assumption was made for the observed number of cases, leading to "exact" 95% confidence intervals (95% CIs) for the SIRs.<sup>3</sup>

Within what appears from available workplace data to be an overall low exposure situation, job codes have been ranked by a committee of occupational hygienists of the Australian petroleum industry, producing seven categories representing increasing potential for exposure to total hydrocarbons. Comparisons of incidence of cancer between exposure levels were made by computing relative incidence rates (RIRs) adjusted for age and smoking habit against "office" as the baseline or least exposed category. Statistical estimates of trend have been made. These analyses use log linear models, again with a Poisson assumption.<sup>4</sup> The calculations were made using GLIM.<sup>5</sup>

Internal comparisons of incidence of cancer between epochs of first employment in the industry have also been made with 1975 and later as baseline.

#### Results

ALL SITE INCIDENCE OF CANCER

This paper reports the cancer incidence state of the male cohort at 31 December 1989 when 50 254 person-years were available for analysis. One hun-

dred and fifty two incident cancers had occurred, SIR 0.99 (95% CI 0.84–1.16).

## SITE SPECIFIC INCIDENCE OF CANCER

Analysis of incidence of cancer by major anatomical site (table 1) showed a deficit for lung cancer, the SIR being 0.5 (95% CI 0.3–0.9). For melanoma the SIR was 1.4 (95% CI 0.8–2.1).

Examination of cancers of the lymphatic and haematopoietic tissue showed SIRs that were raised, but not significantly so, for non-Hodgkin's lym-



Relative incidence rate by total hydrocarbon exposure ranking (see text): all site cancer.

Table 2 Lymphohaematopoietic cancer incidence by period of first employment adjusted for age and calendar period of follow up: men

Period of first employment	Cancers	RIR (95% CI)
1975-84	5	1.0
1965–74	9	1.3 (0.4-4.3)
1955-64	6	1.7 (0.3-7.9)
-1954	6	4.0 (0.7–21)

Test for trend, p = 0.11.

phoma and multiple myeloma. For all types of leukaemia, 12 cases were found compared with 3.6 expected giving a resulting SIR of 3.4 (95% CI 1.7–5.9); of these, seven cases were myeloid leukaemia compared with the 1.8 expected.

# Internal comparisons of occupational exposures

At present data are insufficient to permit examination of the relation between exposure to hydrocarbons and incidence of lymphohaematopoietic cancer or melanoma. Nevertheless the figure shows a modest trend (p = 0.2) for age adjusted all site incidence of cancer to increase with potential exposure category compared with "office" as baseline. In the figure the vertical bars represent 95% CIs; in categories 2 and 5 the numbers of cases were too few for the 95% CIs to be meaningful. In category 3 there were no cases. The dotted line represents the fitting of a smooth curve through these RIRs; the test for trend is derived from this.

No such relation between all site incidence of cancer and epoch of first employment has been found, but table 2 shows a trend (p = 0.11) towards an increase in RIR of all lymphohaematopoietic cancer with earlier first employment.

## Discussion

A review of mortality analyses in part I of the report on this study<sup>2</sup> and the results for incidence of cancer presented here lead to the conclusion that no evidence exists for an overall excess of cancer in employees in the Australian petroleum industry. This conclusion is supported by recent and complete reviews of mortality studies that have been carried out in the industry in other countries.<sup>6-8</sup>

The same may not be true for particular sites as an excess of one of the less common cancers would have little effect on the overall cancer rate. In this cohort an excess of cancers of the lymphohaematopoietic system was found, notably myeloid leukaemia. A nested case-control study has been established to investigate this excess in relation to work exposures.

The possible carcinogenicity of certain compon-

ents and derivatives of crude oil has been the subject of extensive study over the past six decades. Causal associations have been confirmed for several compounds that are common throughout most of the operations of the petroleum industry, such as benzene and four to seven ring polycyclic aromatic hydrocarbons. These are widespread in the community and the industry and include many products of combustion such as benzo-a-pyrene.

In studies on man a causal relation between exposure to benzene and the suppression of bone marrow function has long been recognised.<sup>9-11</sup> Recently investigations of leukaemia among benzene workers have shown increased risk of multiple myeloma and other lymphoid malignancies.<sup>12-16</sup> Although animal studies have provided evidence of the haematotoxic effects of benzene at various concentrations<sup>17-20</sup> considerable doubt remains as to doseresponse relations in man.<sup>8 21</sup> Risk assessment studies<sup>12-23</sup> have projected estimates of leukaemogenic effects at concentrations as low as one part per million, but effects on man of such low concentrations have yet to be shown.

In the Australian petroleum industry changing technology has resulted in lower exposures generally, and to benzene in particular, over the past 40 years. These changes have come about not only through a higher management profile given to occupational health matters, but also for reasons of enhanced productivity, control of product loss, energy conservation, and government imposed control measures for air pollution. New plant is designed in the knowledge that recommended hygiene standards are strict and will become more so; product is more valuable than ever and consequently leaks and spills are guarded against; energy conservation measures also tend to recycling of former waste through plant systems. Bottom loading of transport tankers and floating roof tanks are some specific changes that have occurred throughout the industry and have led to reduced exposure of employees to petroleum products.

The effects of such engineering changes on exposure of employees are difficult to quantify and are spread over long time frames. It is generally agreed within the Australian industry that since the mid-1970s employee exposure to hydrocarbons in general, and benzene in particular, has been reduced substantially.

The trend towards an increase in RIR for lymphohaematopoietic cancers with earlier first employment shown in the Health Watch cohort is difficult to interpret. No such relation was found for all site cancer, and it cannot be determined from the present data whether the relation shown between incidence of lymphohaematopoietic cancer and epoch of first employment indicates decreasing risk with more recent employment, or whether it is a result of a long latency or perhaps an effect of cumulative exposure. Such a distinction will be more amenable to multivariate analysis when the programme has covered more calendar years. The data available at present do justify the continuing efforts being made to engineer exposure out of the workplace, and afford no grounds for complacency.

Health Watch is supported by a grant from the Australian Institute of Petroleum. We are grateful to members of the Occupational Hygiene Committee of the Institute for their assistance in classification of exposure and to personnel staff in participating companies for their continuing commitment to follow up. We recognise the valuable contributions of Anne Potter, Arlene Baade, and Carole Webley in acquisition and management of data.

Requests for reprints to: Mrs K Robinson, Department of Community Medicine, 159 Barry Street, Carlton 3053, Australia.

- 1 Schottenfeld D, Warshauer ME, Zauber AG, Meikle JG, Hart BR. A prospective study of morbidity and mortality in petroleum industry employees in the United States---a preliminary report. In: Peto R, Schneiderman M, eds. Banbury report 9: quantification of occupational cancer. Cold Spring Harbor, New York: Cold Spring Harbor Laboratory, 1981:247-65.
- 2 Christie D, Robinson K, Gordon I, Bisby J. A prospective study in the Australian petroleum industry. I Mortality. Br J Ind Med 1990;48:507-10.
- 3 Liddell FDA. Simple exact analysis of the standardised mortality ratio. J Epidemiol Community Health 1984;38:85-8.
- 4 Berry G. The analysis of mortality by the subject-years method. Biometrics 1983;39:173-84.
- 5 Baker RJ, Nelder JA. The GLIM system, release 3. Oxford, Numerical Algorithms Group, 1979.
- 6 Harrington JM. The health experience of workers in the petroleum manufacturing and distribution industry. The Hague, Netherlands: Concawe, 1987. (Report No 2.)

- 7 Wong O, Raabe GK. A critical review of cancer epidemiology in petroleum industry employees, with a meta-analysis by cancer site. Am J Ind Med 1989;15:283–310.
- 8 Alderson M. Occupational cancer. 1st ed. London: Butterworth, 1986:142-6.
- 9 Aksoy M. Benzene Hematotoxicity. In: Aksoy M, ed. Benzene carcinogenicity. Boca Raton, Florida: CRC Press Inc. 1988: 59-112.
- 10 Young NS. Benzene and Lymphoma (editorial). Am J Ind Med 1989;15:495-8.
- 11 McMichael AJ. Carcinogenicity of benzene, toluene and xylene: epidemiological and experimental evidence. In: Fishbein L, O'Neill IK, eds. Environmental carcinogens: methods of analysis and exposure measurement. Lyon: International Agency for Research on Cancer, 1987:3-18. (Sci publ No 85.)
- 12 Rinsky MS, Smith AB, Hornung R, et al. Benzene and leukaemia: an epidemiologic risk assessment. N Engl J Med 1987;316:1044-50.
- 13 Wong O. An industry wide mortality study of chemical workers occupationally exposed to benzene. I. General results. Br J Ind Med 1987;44:365-81.
- 14 Wong O. An industry wide mortality study of chemical workers occupationally exposed to benzene. II. Dose response analyses. Br J Ind Med 1987;44:382-95.
- 15 Decouffe P, Blattner WA, Blair A. Mortality among chemical workers exposed to benzene and other agents. *Environ Res* 1983;30:16-25.
- Arp EW, Wolf PH, Chekoway H. Lymphocytic leukaemia and exposures to benzene and other solvents in the rubber industry. J Occup Med 1983;25:598-602.
  Baarson KA, Snyder CA, Albert RE. Repeated exposure of
- 17 Baarson KA, Snyder CA, Albert RE. Repeated exposure of C57B1 mice to inhaled benzene at 10 ppm markedly depressed erythropoietic colony formation. *Toxicol Lett* 1984;20:337–42.
- 18 Rozen MG, Snyder CA, Albert RE. Depressions in B- and Tlymphocyte mitogen-induced blastogenesis in mice exposed to low concentrations of benzene. *Toxicol Lett* 1984;20:343-9.
- 19 Snyder CA, Goldstein BD, Sellakumar A, et al. Hematotoxicity of inhaled benzene to Sprague Dawley rats and AKR mice at 300 ppm. J Toxicol Environ Health 1978;4:605–18.
- 20 Snyder ČA, Goldstein BD, Sellakumar AR, Bromberg I, Laskin S, Albert RE. The inhalation toxicology of benzene: incidence of haematopoietic neoplasms and hematotoxicity in AKR/J and C57BL/6J mice. *Toxicol Appl Pharmacol* 1980;54:323-31.
- 21 Jacobs A. Annotation: benzene and leukaemia. Br J Haematol 1989;72:119-21.
- 22 Austin H, Delzell E, Cole P. Benzene and leukaemia: a review of the literature and a risk assessment. Am J Epidemiol 1988; 127:419-39.
- 23 Infante PF, White MC. Projections of leukaemia risk associated with occupational exposure to benzene. Am J Ind Med 1985; 7:403-13.

Accepted 17 December 1990